

## Perinatal Mortality According to Level of Perinatal Healthcare Institutions in Low Birth Weight Infants: Cross Sectional Multicentric Study

### Abstract

**Background:** To investigate the total survival of low birth weight infants (LBWIs) in the Federation of Bosnia and Herzegovina (FB and H) and selected by subgroups of birth weight (BW) and gestational age (GA). **Methods:** This cross-sectional study included newborns of both genders, GA of 22–42 weeks and BW of less than 2500 g of 10 cantons territory of the FB and H. In the examined period, 22,897 children were born in the FB and H, of which 669 (2.9%) had BW less than 2500 g. **Results:** Surviving of LBWIs in the FB and H out of the 669 LBWIs in the first level perinatal healthcare institutions (PHI) was 29 (4.3%), the second level was 286 (42.8%), and the third level was 354 (52.9%). The total stillborn rate was 3.9%. The overall perinatal mortality rate for all levels of PHI was 8.6%. The overall rate of early neonatal mortality of LBWIs in all three levels of PHI in the FB and H was 12.7%. By the end of the first month of life (up to 28 days) and to the end of the neonatal period, 385 (57.5%) of LBWIs survived, and 284 (42.4%) died. The LBWIs by subgroups of BW up to 28 days had lower survival rates in second-level PHI than infants of the same BW subgroups (500–999 and 1000–1499) treated in third-level PHI ( $P = 0.0089$  and  $P = 0.004$ ). **Conclusions:** Our results show that B and H belongs to developing countries according to perinatal mortality. A unique database system is necessary to follow progress and trends.

**Keywords:** *Developing countries, gestational age, infant mortality, perinatal care, pregnancy*

### Introduction

The low birth weight infants (LBWIs) are newborn with a birth weight (BW) less than 2500 g, regardless of the duration of pregnancy, and this term refers to preterm infants, newborns with intrauterine growth retardation (IUGR), and newborns small for gestational age (SGA).<sup>[1]</sup> These newborns represent a risk group and have a high perinatal mortality rate (PMR).<sup>[1,2]</sup>

PMR ranges from 4–7/1000 live births in developed countries, 39/1000 in South America, 53/1000 in Asia to 757/1000 in Africa.<sup>[3]</sup> In comparison with Finland, the European country with one of the lowest PMR (6.3/1000), Federation of Bosnia and Herzegovina (FB and H) has higher PMR which is 8.6/1000.<sup>[3]</sup>

The major causes of the drastic reduction in PMR in our country and globally are an increase in the proportion of births in maternity wards to 99%, comprehensive regionalization of the transport of endangered newborns, and strong public support for

pregnant women and children.<sup>[4,5]</sup> Professional organizations and United Nations agencies need to engage national governments to endorse and support the deployment of mother-baby friendly birthing facilities initiative that will reduce inequalities of care across countries and regions worldwide. With this initiative, improvement in the quality of care could lead to a reduction in maternal and newborn morbidity and mortality. These policies and proposed changes are of low cost and can be implemented in low- and high-resource countries.<sup>[4-6]</sup>

The PMR is a reflection of the quality of health care during pregnancy, childbirth, and the newborn period.<sup>[7]</sup> To monitor the effectiveness of perinatal care, comparisons of PMR are performed over time periods in a particular region or country.<sup>[8]</sup> The PMR can differ even within one country because it depends on numerous factors including the enlightenment, hygienic, and socioeconomic development of society and the individual, the level of education, maternal health prepregnancy, mother's age, parity and marital status, urban or rural residence, health indicators of pregnancy

Enida Nevačinović,  
Anis Cerovac<sup>1,2</sup>,  
Gordana  
Bogdanović,  
Elmedina Cerovac<sup>3</sup>,  
Tvrтко Tupek<sup>4</sup>,  
Haris Zukić

*Clinic for Gynecology and Obstetrics, University Clinical Centre Tuzla, Tuzla, Bosnia and Herzegovina, <sup>1</sup>Department of Gynaecology and Obstetrics, General Hospital Tešanj, Tešanj, Bosnia and Herzegovina, <sup>2</sup>Department of Anatomy, School of Medicine, University of Tuzla, Tuzla, Bosnia and Herzegovina, <sup>3</sup>Department of Anesthesiology, Reanimatology and Intensive Care, General Hospital Tešanj, Tešanj, Bosnia and Herzegovina, <sup>4</sup>Department of Gynecology and Obstetrics, Clinical Hospital "Sveti Duh", Zagreb, Croatia*

### Address for correspondence:

Dr. Anis Cerovac,  
General Hospital Tešanj,  
Braće Pabrić 17, 74260 Tešanj,  
Bosnia and Herzegovina.  
E-mail: a.cerovac@hotmail.com

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and childbirth, and the state of health of the fetus or newborn.<sup>[8]</sup>

The survival of very LBWIs is affected by the place of delivery; survival is greater and morbidity is less likely if infants are born in third level perinatal healthcare institution (PHI) comparing to other places.<sup>[9]</sup>

The aim of this study was to investigate perinatal mortality according to the level of PHIs in LBWIs in the FB and H and divided by subgroups of BW (500–999 g, 1000–1449 g, 1500–1999 g, 2000–2499 g) and GA.

## Patients and Methods

### Patients and study design

This cross-sectional study included newborns of both genders, GA from 22 to 42 weeks, and BW less than 2500 g, born in maternity wards in 10 cantons of the FB and H.

All newborns are classified in one of the three groups based on the GA:

Group 1: preterm neonates (GA 22–36 weeks), group 2: term neonates (GA 37–41 weeks), and Group 3: post-term neonates (GA  $\geq$  42 weeks). By birth, subgroups of BW for each of the three basic groups were formed: 500–999 g, 1000–1449 g, 1500–1999 g, and 2000–2499 g. Newborns with a BW less than 500 g were not among the live-born.

The survey was approved by the ethics committee of the University Clinical Center Tuzla.

### Methods

Data on the course of pregnancy and childbirth were collected on the basis of available medical records (mother's disease history, partogram), and included the place of delivery (maternity and outside maternity wards). The maternity ward was divided based on a 1-year number of deliveries to this study (first level 1–500 births, second level 501–2000, and third level  $>$  2000 childbirths in 1 year).

Data of the LBWIs in the FB and H were collected on the basis of the available medical documentation, including canton of the childbirth, date and hour of birth, BW (in grams), birth length (in centimeters), GA (completed weeks of gestation), Apgar score (AS) at the 1<sup>st</sup> and 5<sup>th</sup> min (value), date and hour of transfer to the neonatal facility, and neonatal institution where the newborn was transferred.

The analysis covers the duration of hospitalization and the outcome of the newborn.

For the purposes of this research, the levels of the neonatal unit were defined according to the diagnostic and therapeutic possibilities, and according to the definition of the Association of Neonatologists of the FB and H from

2000.<sup>[1]</sup> The regional distribution of maternity and neonatal units respected the current status of the organization and usual postnatal transport practice: first level—possibility of care for term eutrophic infants; second level—possibility of care for newborns with hyperbilirubinemia, hypoglycemia, and acidosis; third level—the possibility of taking care of all health problems in infants of any GA and BW including mechanical ventilation, eksangvino transfusion, and all surgical procedures other than cardiac surgeons.<sup>[1]</sup>

In some cantons, there was only a maternity hospital without a neonatal institution, so that the place of birth and care for LBWIs were referred to as PHI by levels.

The preferred time of transport within 4 h of birth was considered.<sup>[1]</sup>

In the newborn period, two health-statistical categories are distinguished: early neonatal mortality rate (ENMR) (death in the first 7 days of life or up to 168 h of life), and neonatal mortality (death in the first 28 days of life), including those newborns dying in the first 7 days of life.<sup>[8]</sup> Data on mortality and survival were reported as PMR (stillborn and deceased up to 7 days of life). It consists of late fetal mortality (LFM) and ENMR. This connection is justified because many circumstances are related to LFM equal to or similar to ENMR.<sup>[8]</sup>

### Statistical analysis

Descriptive statistics, mean value, standard deviation (SD), and coefficient of variation (CV) were used in the statistical data processing. Quantitative data were intergrouped with the Mann-Whitney U test, and qualitative data were compared with the  $\chi^2$  test and the Fisher's exact test. The prediction power of the BW, GA, birthplace in predicting the results of the treatment was determined by specificity, sensitivity, positive and negative predictive value, and a multiple regression analysis was used to compare the two dependent on one independent variable. Statistical significance was determined at the level of the difference of 5% and 1%.

## Results

In the examined period, 22,897 children were born in the FB and H, of which 669 (2.9%) had BW less than 2500 g. Of the 669 LBWIs, 29 (4.3%) were born in the first level of PHI, 286 (42.8%) in the second level, and 354 (52.9%) in the third level.

The stillborn rate in the first level PHI was 22/1651 (13.32%), 26/9490 (2.74%) in the second level, and 42/11666 (3.60%) in the third level. The total stillborn rate was 3.9%. In the first 7 days of life, none of the LBWIs survived in first level PHI. In the second PHI level, 54 (10.5%) LBWIs survived in the first 7 days of life ( $P = 0.398$ ). In third level PHI, 461 (89.5%) of LBWIs survived in the first 7 days. In relation to survival

in the second level PHI, the difference was statistically significant ( $P < 0.0001$ ).

The PMR in the first level PHI was 15.1%, primarily at the expense of stillbirths, and it significantly affected overall PMR of 8.6 (or 4.71%) for all levels of PHI, and it was almost identical (or similar) to the PMR of the second (8.3%) and the third PHI (8%). Total PMR was increased due to ENMR, which was in favor of a larger number of deceased newborns in the first 7 days of life compared to the number of stillbirths. A statistically significant difference in PMR was found only in the comparison of the first level with the other two levels of PHI ( $P = 0.006$ ) (OR = 1.893; 95% CI [1.214–2.951]).

In the first level PHI, three LBWIs (out of 643; 0.5%) were treated, and three (out of 108; 2.8%) died in the early neonatal period. The ENMR for LBWIs in the first PHI level was 1.8%.

In the second PHI level, 127 (out of 286; 19.7%) of LBWIs were detected, of whom 53 (18.5%) died in the early neonatal period. The ENMR of LBWIs in the second PHI level was 5.6%.

In third level PHI, 513 (out of 643; 79.8%) of LBWIs were treated, 461 were survived, and 52 (14.6%) died in the early neonatal period. The ENMR for LBWIs at third level PHI was 4.5%. A statistically significant difference was not found in the mortality of LBWIs between the first and second levels of PHI ( $P = 0.398$ ) (RR = 0.507; 95% CI [0.148–1.738]). A significant statistical difference was found in the rate of the death of LBWIs between PHI at the second and third levels ( $P < 0.0001$ ) with a high relative risk (RR = 6.349; 95% CI [4.030–10.003]). The overall ENMR of newborns with lowest BW at all three levels of PHI was 4.7%, and the highest one was in the PHI of the second level.

During the early neonatal period, 108 (out of 669 (16.1%) of LBWIs died, and by the end of the 1<sup>st</sup> month of life

(up to 28 days of life), another 176 (26.3%) died, resulting in the total of 284 (out of 669 [42.4%]) of dead LBWIs.

Up to 28 days of life, 284 (out of 669 [42.4%]) LBWIs died, of which 169 (out of 669 (25.3%) died in the third level of PHI, 112 (out of 669 (16.7%) in the second PHI level, and three (out of 669 (0.4%) in the first PHI level.

Surviving rate of LBWIs was 57.5% (385 out of 669) in the second-level institutions and 43.6% (292 out of 669) in the third-level institutions (no survivors in the first-level institutions). Statistically significant differences in the survival of LBWIs were not found in PHI of the second level with almost equal chances for survival and death ( $P = 0.171$ ) (OR = 1.125; 95% CI [0.923–1.678]). A statistically significant difference in the survival of LBWIs was found in PHI of the third level ( $P < 0.0001$ ) (OR = 0.436; 95% CI [0.346–0.550]). The overall ENMR of LBWIs in all three PHIs in the FB and H was 12.7% [Table 1].

By the end of the 1<sup>st</sup> month of life (up to 28 days) and the end of the neonatal period, 385 (57.5%) of LBWIs survived, and 284 (42.4%) died ( $P = 0.0001$ ) (OR 1.83795% CI [1.479–2.282]) [Table 2].

The LBWIs by subgroups of BW up to 28 days according to the level of PHI in which they were treated had lower survival rates in second PHI level than infants of the same BW subgroups (500–999 and 1000–1499) treated in third-level PHI ( $P = 0.0089$  and  $P = 0.004$ ), whereas this difference was not found in the larger BW subgroups [Table 3].

Survival of LBWIs by subgroups of the GA up to 28 days according to the level of PHI in which they are treated is the lowest in the lowest GA (22–26), but without statistical significance ( $P = 0.107$ ) on contrary to the highest GA (36 and more) ( $P = 0.014$ ) [Table 4].

The difference in survival of LBWIs selected according to the GA and according to the PHI of treatment pointed

**Table 1: The time of death of low birth weight infants (LBWIs) per levels of perinatal healthcare institutions (PHIs)**

Level PHI	No (%) of newborns according to the time of death				Total
	<12 h of life	12.01-24.00 h of life	24.01-168.00 h of life	168.01-672.00 h of life	
I	3 (3)	0	0	0	3
II	34 (30.4)	7 (6.25)	12 (10.7)	59 (52.7)	112
III	19 (11.2)	27 (15.9)	6 (3.6)	117 (69.2)	169
Total	56 (19.7)	34 (11.9)	18 (6.3)	176 (61.9)	284

**Table 2: Survival of LBWIs by subgroups of birth weight (BW) up to 28 days of life**

BW (grams)	No (%) of LBWI newborns		Total	P	OR (95% CI)
	Survived up to 28 days	Died up to 28 days			
500-999	21 (5.4)	28 (9.8)	49	0.225	0.562 (0.252-1.252)
1000-1449	69 (61.6)	43 (38.4)	112	0.0008	2.574 (1.502-4.412)
1500-1999	92 (52.6)	83 (47.4)	175	0.392	1.228 (0.807-1.869)
2000-2499	203 (60.9)	130 (39.1)	333	0.0001	2.438 (1.786-3.329)
Total	385 (57.5)	284 (42.5)	669	0.0001	1.837 (1.479-2.282)

that survival in the subgroup of the lowest GA (22–26) was similar in the second- and third-level PHI ( $P = 0.60$ ) in contrast to 27–29 GA subgroup, where survival was significantly higher in third-level PHI compared to second-level PHI ( $P = 0.003$ ) [Table 5].

Survival of LBWIs born and treated in PHI of the third level is significantly higher (43.6%) than survival and treatment of LBWIs at PHI of the second level (13.9%) ( $P < 0.0001$ ). The survival rate of LBWIs transferred to the third PHI level was 56% (89 out of 159) ( $P < 0.0001$ ; Fisher's exact test  $P = 0.00002$ ) (compared with the survival of LBWIs born and treated in PHI of the second level)

## Discussion

Despite evident progress in perinatology and significant improvement in perinatal outcome over the past decade, LBWIs remain a major problem in the world and dominant risk factor for infant mortality and/or for subsequent permanent damage.<sup>[1]</sup>

The results of this study showed 42.4% of LBWIs died and 57.5% survived. LBWIs were less likely to die in the first 7 days of life than in the period after 7 days. In the second level PHI, most of the LBWIs died in the first 12 h after birth, while in the third level after 168 h of life.

The dying pattern of the newborns who did not survive until the end of the neonatal period in our study is similar to that one of the developed countries, probably because of the availability of the third level PHIs and dying is prolonged.<sup>[10]</sup> Significantly better survival of LBWIs was recorded in Croatia in 2003 in all LBWIs subgroups.<sup>[11]</sup> The establishment of intensive care units for newborns, prenatal, and postnatal transport of newborns, or the implementation of basic settings of regionalization of perinatal health care, resulted in a reduction in ENMR, morbidity and disability.<sup>[6,10]</sup> However, everywhere in the world the question arises as to whether the reduction in ENMR is a consequence of delayed mortality or whether the impact of medical advancement in intensive care units for newborns resulted in the postponement of the death of newborns, which was therefore not reported in ENMR or in PMR.<sup>[10]</sup> An important novelty in the prevention of PMR is that in our country the survival of very low and extremely LBWIs (under 1000 and 1500 g) is gradually increasing. In this group of neonates, the proportion of later complications is high in the late neonatal and postneonatal period, and it is important to monitor their long-term survival or at least survival until discharge from the hospital.<sup>[12]</sup> That is why late neonatal mortality, or mortality until discharge from the hospital, is a more complete measure of neonatal and

**Table 3: Outcome of LBWIs in PHIs of the second and third levels by subgroups of BW up to 28 days of life**

BW	No (%) of LBWI newborns at PHI II level		No (%) of newborns at PHI III level		P
	Survived	Died	Survived	Died	
500-999	4 (4.3)	17 (15.1)	17 (5.8)	11 (6.5)	0.008
1000-1449	26 (27.9)	29 (25.9)	43 (14.7)	14 (8.3)	0.004
1500-1999	28 (30)	36 (32.1)	64 (21.9)	47 (27.8)	0.105
2000-2499	35 (37.6)	30 (26.8)	168 (57.5)	97 (57.3)	0.202
Total	93 (100)	112 (100)	292 (100)	169 (100)	<0.0001

**Table 4: Outcome of LBWIs by subgroups of gestational age (GA) up to 28 days of life**

GA	No (%) survived LBWIs	No (%) died LBWIs	No (%) total	P	OR (95% CI)
22-26	8 (38.1)	13 (61.9)	21 (100)	0.107	0.442 (0.180-1.082)
27-29	47 (63.5)	27 (36.5)	74 (100)	0.329	1.323 (0.802-2.182)
30-32	81 (65.3)	43 (34.7)	124 (100)	0.065	1.493 (0.994-2.242)
33-35	105 (61)	67 (39)	172 (100)	0.323	1.214 (0.852-1.730)
36	144 (51.8)	134 (48.2)	278 (100)	0.014	0.668 (0.489-0.913)
Total	385 (57.5)	284 (42.4)	669 (100)	0.0001	1.837 (1.479-2.282)

**Table 5: Outcome of low birth weight infants (LBWIs) in PHIs of the second and third levels by subgroups of the GA up to 28 days of life**

GA	No (%) of LBWI newborns at PHI II level		P	No (%) of LBWI newborns at PHI III level	
	Survived	Died		Survived	Died
22-26	2 (2.1)	9 (8)	0.60	6 (2)	4 (2.3)
27-29	5 (5.3)	18 (16.1)	0.003	42 (14.3)	9 (5.3)
30-32	26 (27.9)	29 (25.9)	0.006	55 (18.8)	14 (8.2)
33-35	23 (24.7)	21 (18.7)	0.0001	82 (28.1)	46 (27.2)
36	37 (39.8)	35 (13.4)	0.0001	107 (36.6)	96 (56.8)
Total	93 (100)	112 (100)	0.0001	292 (100)	169 (100)



pediatric service performance than ENMR. It is estimated that 3.7 million newborns die worldwide in the first 28 days after birth and 3 million are stillborn.<sup>[13-15]</sup>

In our study, the survival of LBWIs depended on the level of the PHI and it increased with the greater organizational level. The survival of LBWIs in our study significantly differed according to the levels of the PHI of birth, weight groups, and GA. GA itself does not provide enough information to predict the child's condition at birth, as many other causes change the outcome of the newborn.<sup>[16-18]</sup> The results of our study have shown that with the rise of pregnancy age, the chances of surviving LBWIs at the second level of PHI were increasing, but only after 30 gestational weeks when survival was 27.9% in neonatal institutions of the second level, which confirms our hypothesis.

Stillbirths, early neonatal mortality, and perinatal mortality were lower in our study in the comparison with the period during the war (1992–1995) in study Skokić *et al.*, but higher than in pre- and postwar periods.<sup>[1,19,20]</sup> In comparison with the study by Sun *et al.*, the stillbirth rate is the same as in our study (3.9%) but perinatal mortality is slightly lower than in our study (7.7% vs 8.6%), respectively.<sup>[21]</sup>

The significance of our study is that there are several studies on perinatal mortality in FB and H, but our study was the first one investigating perinatal mortality in LBWIs. The strength of the study is cross-sectional and multicenter data collection with standards of the primary to the tertiary level of care. This report is our first attempt to cross-sectional conduct a multicentric survey of the perinatal mortality of LBWIs in FB and H.

## Conclusions

The most important factor in order to successfully reduce neonatal mortality is political will. In the meantime, we must continue to develop new strategies to lower the mortality risk of LBWIs. For neonatal mortality, this endeavor will include reducing the risk of low BW, providing adequate family planning services to reduce unwanted pregnancies, renewing efforts to provide timely and appropriate perinatal health care, regular health care during pregnancy, and skilled attendance at delivery. Our results show that Bosnia and Herzegovina fall under developing countries according to perinatal mortality. A unique database system is necessary to follow progress and trends.

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## Conflicts of interest

There are no conflicts of interest.

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